

## REMARKS

### 1. Preliminary Remarks

#### a. Status of the Claims

Claims 26, 31, 33, and 35-37 are pending in this application. Claims 31, 33, 35, 36, and 37 are amended. Claims 1-25, 27-30, 32, 34, and 38-40 had been previously canceled. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the application. Upon entry of the amendments, claims 26, 31, 33, and 35-37 will be pending and under active consideration.

#### b. Amendments to the Claims

Claim 35 is amended in part to be directed to an isolated nucleic acid wherein the sequence of the nucleic acid consists of (a) SEQ ID NO: 117937; (b) a DNA encoding the nucleic acid of (a), wherein the DNA is identical in length to (a); (c) a sequence at least 80% identical to (a) or (b), wherein the nucleic acid is 19-24 nucleotides in length; and (d) the complement of (a)-(c) wherein the complement is identical in length to the nucleic acid of (a)-(c). Support for 80% variants of SEQ ID NO: 117937 wherein the nucleic acid is 19-24 can be found throughout the specification, for example, paragraphs [0054] and [0274].

Independent claims 31 and 36 have been amended to be directed to a vector comprising a heterologous sequence, wherein the heterologous sequence consists of the nucleic acid of claim 26 or 35. Independent claims 33 and 37 have been amended to be directed to a probe comprising a heterologous sequence, wherein the heterologous sequence consists of the nucleic acid of claim 26 or 35. Support for claims 31, 33, 36, and 37 can be found throughout the specification, for example, paragraph 0035, which is set forth below.

Accordingly, the invention provides several substantially pure nucleic acids (e.g., genomic DNA, cDNA, or synthetic DNA) each comprising a novel GAM oligonucleotide, vector comprising the DNAs, probes comprising the DNAs, a method and system for selectively modulating translation of known target genes utilizing the vectors, and method and system utilizing the GAM probes to modulate expression of GAM target genes.

Vectors are well known to be useful for many purposes, including the transfer of a nucleic acid of interest. The nucleic acid of interest is considered to be "heterologous" with respect to the basic construct of a vector. The above provided passage of paragraph 0035 of the specification

clearly shows that a vector is contemplated that includes a nucleic acid of interest such as the subject matter of claims 26 or 35. One of ordinary skill in the art would recognize that features heterologous to the nucleic acid of claim 26 or 35 would be necessary for a functional vector.

Probes are well known to be useful for purpose including the hybridization and detection of a nucleic acid of interest. Hybridization is typically accomplished by using a sequence that is sufficiently complementary to the target sequence. The hybridization sequence is considered to be “heterologous” with respect to the basic construct of a probe useful for detection. The above provided passage clearly shows that a probe is contemplated that includes a hybridization sequence, such as the subject matter of claims 26 or 35. One of ordinary skill in the art would recognized that features other than the heterologous sequence would be necessary for identifying whether the probe bound to a complementary sequence.

**c. Objection to the Specification**

On page 2 of the Office Action, the Examiner maintains the objection to the specification requiring that specification be amended under 37 C.F.R. §1.52(e)(5) to include all portions of Tables 1-14 that specifically deal with SEQ ID NOS: 4204050 and 117937, and in particular the portions of Tables 8 and 9, which disclose the identity and functions of the genes or genes targeted by SEQ ID NOS: 4204050 and 117937. As provided in the Amendment to the Specification, the Applicant hereby adds the relevant portions of Tables 1-9 into amended paragraphs [0209]-[0214] as they relate to the claimed invention. Support for amended paragraphs [0209]-[0214] can be found in the table below.

Amended Paragraph	Support in the Specification	Support from Incorporated Tables
[209] (Tables 1-3)	[493]-[495]	Table 1, lines 241237; Table 2, lines 4474648-4474741; Table 3, lines 320140-320141
[210] (Table 4)	[496]	Table 4, lines 599770-599773
[211] (Table 5)	[497]	Table 5, lines 239916-239917
[212] (Tables 6 and 7)	[498] and [499]	Table 6 shows data relating to the SEQ ID NO: of the GAM target binding site sequence to the TARGET gene name as bound by the GAM RNA as set forth in SEQ ID NO: 1179376. Table 6, lines 2093282 and 2093283 relate to target binding site SEQ ID NO:

		2034243; lines 6630926 and 6630927 relate to target binding site SEQ ID NO: 3983175; lines 2093540 and 2093541 relate to target binding site SEQ ID NO: 2034310; lines 6638580 and 6638581 relate to target binding site SEQ ID NO: 3985198; line 6630929 relates to target binding site SEQ ID NO: 3983175; line 2093543 relates to target binding site SEQ ID NO: 2034310; line 6638583 relates to target binding site SEQ ID NO: 39851980; lines 2087866 and 2087867 relate to target binding site SEQ ID NO: 2032849; lines 663308 and 663309 relate to target binding site SEQ ID NO: 3983798; and line 2058344 relates to SEQ ID NO: 2024974; Table 7, lines 6493595-6493625.
[213] (Table 8)	[500]	Table 8, lines 4766438-4766618
[214] (Table 9)	[501]	Table 9, lines 40832-40882

Applicant submits that no new matter is added to the specification as all amendments to paragraphs [0209]-[0214] draw support from other parts of the specification. Applicant submits that the amendments address the Examiner's requirement under 37 C.F.R. §1.52(e)(5) and therefore request that the objection has been overcome.

**d. Objection to the Claims**

On page 3 of the Office Action, the Examiner rejects claims 31, 33, 36, and 37 under 37 C.F.R. §1.75(c) as being in improper dependent form for failing to further limit the subject matter of the previous claim. In view of the foregoing amendments in which all claims have been amended into independent form, Applicant submits that the objection is now moot and requests withdrawal of the objection.

**e. Interview Summary**

The undersigned would like to thank the Examiner for the courtesy of the telephone interview on February 26, 2009, wherein the obviousness rejection and possible claim amendments were discussed. The new claims provided herein are reflective of the possible amendments proposed in the interview. Based on the interview, Applicant believes that the application is in condition for allowance.

**2. Patentability Remarks****a. 35 U.S.C. § 112, first paragraph**

On page 4-6 of the Office Action, the Examiner rejects claims 31, 33, 36, and 37 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Examiner asserts that new matter has been added because there is no support in the specification for the exclusion of viral sequences from the vectors or probes. In view of the foregoing amendment to the claims, Applicant submits that the specification provides distinguishing characteristics that would allow one of skill to identify the heterologous sequence that are comprised within the claims probes and vectors. Accordingly, Applicant respectfully requests that the rejection of claims 31, 33, 36, and 37 under 35 U.S.C. § 112, first paragraph has been overcome and should be withdrawn.

**b. 35 U.S.C. § 103**

On pages 6-11 of the Office Action, the Examiner maintains the rejection of claims 26 and 33 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ghazal (WO200257437; "Ghazal") in view of Hogan (US 5,541,308; "Hogan") and claims 35 and 37 over Ghazal in view of Buck et al., Biotechniques 27:528-536 (1999; "Buck"). Specifically, the Examiner asserts that although at least 8,255,610 possible probes could be created based upon the teachings of Ghazal in view of Hogan or 1,834,676 possible probes could be created based upon the teachings of Ghazal in view of Buck, it is the position of the Office that all these probes and primers are equivalents for the purpose of probing or priming the sequences of Ghazal, and absent secondary considerations, are therefore obvious over each other. The Examiner further asserts that the Applicant's assertion that the claimed oligonucleotides function as or are related to miRNAs does not rise the level of secondary consideration because there is no evidence that the claimed sequences have miRNA or gene regulatory activity. Applicant respectfully disagrees.

Applicant submits that the specification teaches that the claimed miR, which is a human herpesvirus 5 or more commonly known as human cytomegalovirus (HCMV) regulates the

immediate-early 1 (IE-1) gene transcript of HCMV at Table 7, lines 6,493,606-6,493,610 and as amended, at the paragraph [0212] of the specification as depicted below.

GAM NAME	GAM ORGANISM	GAM RNA SEQUENCE	TARGET BS-SEQ	TARGET REF-ID	TARGET ORGANISM	UTR	BINDING SITE TARGET; LOWER: GAM)	DRAW (UPPER: GAM)	GAM POS
=====	=====	=====	=====	=====	=====	=====	=====	=====	=====
GAM501831	Human herpes virus 5	AGTGACGG TGAGATCC AGGCTG	GCTGATCG CCGTCAC	NC_0013 47 1906 93237 - 193 96 - 19 637 3236 gene	NC_001347 1 Human herpes virus 5	3	-- - - G-- GC TG ATC CCGTCACT CG AC TAG GGCAGTGA GT G C AGT		A

Applicant further submits that the claimed miR is miR-UL112-1 as discussed in Murphy *et al.*, *PNAS* 105:5453-5458 (2008) (see Figure 1). HCMV miR-UL112 is shown in Murphy to bind and regulate miRNA expression of HCMV's immediate-early (IE-1) gene. Murphy confirms the teachings of the specification that the IE-1 gene of HCMV is regulated in trans by the claimed miR (miR-UL112-1) (SEQ ID NO: 117937). This evidence provides the secondary consideration that the claimed miR unexpectedly regulates a gene in trans and is therefore distinguishable and unique amongst the 8,255,610 or 1,834,676 possible probes or primer that could be arrived at based upon the teachings of Ghazal in view of Hogan or Buck respectively. Based upon these results, Applicant submits that the claimed miR and related hairpin sequences are not obvious over Ghazal in view of Hogan or Buck. In view of the foregoing amendment and remarks, Applicant submits that the rejection of claims 26, 33, 35, and 37 under 35 U.S.C. §103(a) as being unpatentable over Ghazal in view of Hogan or Buck has been overcome and should be withdrawn.

### 3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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